

Claims

1. A polypeptide comprising a PDE polypeptide sequence with an amino-terminal deletion, said polypeptide exhibiting decreased aggregate formation.
2. The polypeptide of claim 1, wherein said PDE polypeptide sequence is a long form PDE polypeptide sequence.
3. The polypeptide of claim 1, wherein said PDE polypeptide sequence is a PDE4 polypeptide sequence.
4. The polypeptide of claim 3 wherein said PDE polypeptide sequence is a PDE4D polypeptide sequence.
5. The polypeptide of claim 4 wherein the proportion of non-aggregated polypeptide in the total polypeptide is from 55% to 100% of total polypeptide.
6. The polypeptide of claim 1 wherein the proportion of non-aggregated polypeptide in the total polypeptide is from 55% to 100% of total polypeptide.
7. The polypeptide of claim 1, wherein the polypeptide sequence starts at any amino acid located between the LF1 splice site and the first amino acid of the UCR1 start of the native PDE polypeptide.
8. The polypeptide of claim 7, wherein the polypeptide sequence starts at the LF1 splice site of the native PDE polypeptide.
9. The polypeptide of claim 7, wherein the PDE polypeptide sequence start is located 13 amino acids upstream of the UCR1 start of the native PDE polypeptide.

10. The polypeptide of claim 4 wherein the PDE4D polypeptide sequence is a sequence of an isoform selected from the group consisting of D3, D4, D5, D6, D7, and D8.
11. The polypeptide of claim 1 wherein said polypeptide comprises one or more mutations of Serine residues.
12. The polypeptide of claim 11 wherein said Serine residues are mutated to either Alanine or Aspartic acid.
13. The polypeptide of claim 11 wherein said Serine residues are selected from the group consisting of Ser54 and Ser579.
14. The polypeptide of claim 1 wherein said polypeptide exhibits decreased tubulin association.
15. A polynucleotide sequence encoding a polypeptide of claim 1.
16. A polynucleotide sequence encoding a polypeptide of claim 2.
17. A polynucleotide sequence encoding a polypeptide of claim 3.
18. A polynucleotide sequence encoding a polypeptide of claim 4.
19. A polynucleotide sequence encoding a polypeptide of claim 5.
20. A polynucleotide sequence encoding a polypeptide of claim 6.
21. A polynucleotide sequence encoding a polypeptide of claim 7.
22. A polynucleotide sequence encoding a polypeptide of claim 8.

23. A polynucleotide sequence encoding a polypeptide of claim 9.
24. A polynucleotide sequence encoding a polypeptide of claim 10.
25. An expression vector or virus comprising a polynucleotide sequence as claimed in claim 15 capable of directing expression of the polynucleotide sequence in a compatible prokaryotic or eukaryotic host cell.
26. A virus as claimed in claim 25 wherein the virus is a recombinant baculovirus.
27. A prokaryotic or eukaryotic host cell transformed or infected with the expression vector or virus of claim 25.
28. A host cell of claim 27, wherein the host cell is an insect cell.
29. A prokaryotic or eukaryotic host cell transformed or infected with the expression vector or virus of claim 26.
30. A host cell of claim 29, wherein the host cell is an insect cell.
31. A process for the production of a polypeptide of claim 1, comprising culturing the host cell of claim 29 in a suitable medium so that said polypeptide is expressed, and purifying said polypeptide from the cells.
32. A process for the production of a polypeptide of claim 31 wherein the host cell is an insect cell.
33. A process for the production of a polypeptide of claim 1 comprising culturing the host cell of claim 27 in a suitable medium so that said polypeptide is expressed, and purifying said polypeptide from the cells.

34. A process for the production of a polypeptide of claim 33 wherein the host cell is an insect cell.

35. An antibody against a polypeptide of claim 1.

36. An antibody of claim 35, wherein the antibody binds to an epitope of the N-terminal domain of the polypeptide of claim 1.

37. A screening assay for the identification of agonists or antagonists of phosphodiesterase activity comprising at least one polypeptide of claim 1.

38. A process for identifying and obtaining a drug candidate for therapy of an inflammatory disease, said process comprising measuring the activation or inhibition of the phosphodiesterase activity of a polypeptide of claim 1.

39. A compound identified according to the assay of claim 37.

40. A compound identified according to the process of claim 38.

41. A pharmaceutical composition comprising an agonist or antagonist of the phosphodiesterase activity of the polypeptide of claim 1, and a pharmaceutically acceptable carrier.

42. A method of assaying a candidate agonist or antagonist for its ability to interact with a phosphodiesterase comprising crystallizing a polypeptide of claim 1 in a condition suitable for X-ray crystallography and conducting said X-ray crystallography on said polypeptide.

43. A crystallized polypeptide of claim 1.